REMARKS/ARGUMENTS

Claims 13-22 were pending in the instant application. Claims 18 and 21 have been cancelled. Applicants have amended Claim 13 to cognate the elements of previous Claim 21 into revised Claim 13, such that Claim 13 is now a method claim. Text from previous Claim 20 has also been used. Claim 21 has consequently been withdrawn. Claim 13 has also been amended to include the limitations (from page 14, lines 29-30 of the specification), that the preferred dyes have absorption maxima in the range 600-1300 nm. Claim 13 has also been amended to specify that the contrast agent is administered intravenously. Basis can be found in the specification, at page 22, lines 1-3, especially line 3. Consequently, claim 18 has been withdrawn. Claims 14-17 and 19-20 have been amended to method claims, to make them consistent with revised claim 13. Claim 22 has been amended to a method of diagnosis.

1. CLAIM REJECTIONS: 35 USC §112.

Claims 13-22 stand rejected as failing to comply with the written description requirement under 35 USC 112, first paragraph..

Amended Claim 13 is now limited to a method of optical imaging of endometriosis of an animate subject. The claim no longer claims optical imaging contrast agents *per se*. Hence, it can no longer be argued that the claim pertains to compounds defined only by their function.

Applicants contend that the specification provides sufficient information for the person skilled in the art to reproduce the method of amended claim 13. The specification provides

suitable optical reporters; a description of suitable optical imaging techniques at [0117]; plus a description of targeting molecules at [0011-0086], and methods of labelling them with optical reporters at [0101-0102 plus 0118-0128] and Examples 1 to 4. The person skilled in the art can either use the contrast agents described in the specification, or generate new ones. Applicants suggest that the claim scope for such an optical imaging method claim should not be limited by the possible future advent of new targeting molecules. If a person skilled in the art has available a compound with affinity for one of the targets described, then labelling such a compound with an optical reporter is taught by the present specification.

The revised claims are therefore believed to comply with 35 USC §112, and Applicants contend that this rejection over claims 13-22 should be withdrawn.

2. CLAIM REJECTIONS: 35 USC §102.

2.1. Fevig.

Previous claims 13, 16-18 and 21 stand rejected under 35 USC 102 as lacking novelty over Fevig *et al* to J.Med.Chem., 30, 156-165 (1987) (Fevig).

Applicants point out that previously amended claim 13 is now limited to a method. Fevig is silent on the claimed method - the Examiner has acknowledged that already on page 8 of the Office Action. Whilst the compounds of Fevig might potentially be useful in the method, Fevig does not anticipate the method of amended claim 1. Hence, Applicants contend that the novelty rejection to claim 13 should be withdrawn. By definition, revised dependent claims 14-20 are also believed novel over Fevig.

Claim 22 incorporates all the features of claim 13, and is believed novel over Fevig for the same reasons. The novelty rejection based on Fevig should therefore be withdrawn.

2.2. Jallad (US 2003/0162234 A).

Claims 13 and 17-22 stand rejected under 35 USC 102 as lacking novelty over Jallad to US 2003/0162234 A (Jallad).

As for Fevig (see 2.1), claim 13 is now limited to a method of optical imaging of endometriosis. Jallad is silent on endometriosis. Hence, claims 14-20 and 22 are believed novel over Jallad for similar reasons to those given in 2.1. The novelty rejection of claims 13 and 17-22 based on Jallad should therefore be withdrawn.

2.3. Weissleder (US 2003/0044353 A).

Claims 13-21 stand rejected under 35 USC 102 as lacking novelty over Weissleder to US 2003/0044353 A (Weissleder).

As for Fevig and Jallad (see 2.1 and 2.2), Applicants point out that claim 13 is now limited to a method of imaging of endometriosis. Hence, claims 14-20 and 22 are believed novel over Weissleder for similar reasons to those given in 2.1. Applicants also note that the Examiner (p.9) acknowledges that Weissleder does not disclose optical imaging of endometriosis. The novelty rejection of claims 13-21 based on Weissleder should therefore by withdrawn.

3. CLAIM REJECTIONS: 35 USC §103.

3.1. Fevig and Wallace.

Claims 13-18, 20 and 21 are rejected under 35 USC 103 as being unpatentable over Fevig in view of Wallace to US 6,096,874 (Wallace). The logic appears to be that, since Wallace teaches that estrogen receptor – targeting imaging agents "may be useful in the diagnosis of estrogen receptor positive cancers, meningiomas and endometriosis" (column 1), the person skilled in the art would be motivated to use the compounds of Fevig for the same application.

Amended claim 13 specifies that the reporter (R) must have an absorption maximum in the rage 600 to 1300 nm. Fevig at Table IV page 161 describes the characteristics of the fluorophores of the conjugates of Table III. Those show excitation wavelengths (λ_{max}^{excit}) in the range 336 to 490 nm. That is a different range. Hence, even if the person skilled in the art were to combine Fevig and Wallace in the manner suggested by the Examiner, that would lead to subject matter outside the scope of present amended claim 1. Similar logic applies to dependant claims 14 to 20, plus independent claim 22. The obviousness rejection of claims 13-18, 20, and 21 based on [Fevig] + [Wallace] should therefore be withdrawn.

3.2. Weissleder and Schneider.

Claims 13-22 stand rejected under 35 USC 103 as being unpatentable over Weissleder in view of Schneider *et al.* to US 6,387,629 (Schneider).

The Examiner's logic is that the teaching of Weissleder includes a disclosure of activatable optical probes, and that Cathepsin S is one possible target described. Whilst Weissleder does

not disclose optical imaging of endometriosis, Schneider discloses that Cathepsin S is upregulated in endometriosis. The Examiner contends that therefore the person skilled in the art would be motivated to apply the cathepsin targeting probes of Weissleder in the optical imaging of endometriosis.

In response, Applicants point out that Schneider already discloses *in vivo* imaging of endometriosis in a "subject". See Column 3 lines 23-38 of Schneider plus Column 21 lines 22-67 and Claims 33-36. Schneider contemplates *in vivo* imaging using compounds with a "detectable label" (Column 12 lines 27-29). The detectable label is defined at Column 8 lines 32-65, and includes fluorescent dyes. The disclosure of Schneider in that regard (*in vivo* imaging of endometriosis) is limited to laparoscopy, ie. *via* a small surgical incision where "the compound is introduced into the subject at the site of a suspected lesion". [Emphasis added]. See Schneider at Column 21, lines 27-32. Thus, in the context of *in vivo* optical imaging Schneider teaches local administration to the site of disease/lesion. Present amended claim 1 is novel over that approach by specifying intravenous administration.

The combination [Schneider]+[Weissleder] suggested by the Examiner is believed to be an invalid combination. Thus, Schneider already describes *in vivo* imaging but requires use of laparoscopy techniques and administration at the lesion site in the context of optical imaging. Hence, the combination suggested by the Examiner involves contradicting the direct teaching of Schneider itself, and is believed invalid for that reason. Furthermore, Schneider teaches towards the use of radioisotopes or MRI paramagnetic labels as preferred for *in vivo* imaging of endometriosis – see Column 3 lines 32-38 and Column 21 lines 32-37. Hence, Schneider

itself teaches away from the Examiner's combination by teaching towards such quite different imaging modalities for *in vivo* imaging. The present claims are limited to optical imaging, and are believed unobvious over [Schneider]+[Weissleder] for those reasons. Applicants therefore contend that the obviousness rejection of claims 13-22 based on [Schneider]+[Weissleder] should be withdrawn.

4. DOUBLE PATENTING.

Applicants note this provisional rejection over co-pending applications 10/573606, 10/582679, 10/582680, 10/582842 and 10/582893.

Applicants believe that the present amendment limiting to a method of imaging, now distinguishes the subject matter, so that this provisional rejection no longer applies. In the event, however, that the rejection is maintained and the present claims are allowed, Applicants will consider filing a terminal disclaimer as necessary.

CONCLUSION

Applicants respectfully hold that the claims submitted herewith fulfill the requirements of a patentable invention and that all rejections and objections be withdrawn and claims 13-17, 19-20, and 22 be allowed.

The Examiner is invited to telephone the undersigned in order to resolve any issues that might arise and to promote the efficient examination of the current application.

Respectfully submitted,

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